Remarks

Claims 12-17 are pending. Claim 18 has been added. Thus, claims 12-18 are presented for consideration.

Claims 12 and 13 are amended.

Applicants respectfully request reconsideration of the application in view of the claim amendments and the following remarks.

Amendments to the Specification

The Office Action stated an objection to the abstract as being insufficiently informative of the subject matter of the specification. Applicants have amended the abstract. No new matter has been introduced into the application by this amendment.

Amendments to the Claims

Claim 12 has been amended to recite:

A support containing bound target whole cells from a mixture of whole cells, comprising: a support comprising one or more base polymer supports containing an azlactone moiety, a biologically active substance covalently coupled to the support, and target whole cells bound to said substance, wherein the support comprises one or more base polymer supports that have been identified as exhibiting minimal nonspecific binding of non-target whole cells of the mixture of whole cells.

This amendment is fully supported by the specification at, for example, page 5, line 24 through page 6, line 10.

Claim 13 has been amended to correct a typographical error and to conform to claim 12, as amended herein.

Claim 18 recites the method of claim 12 in which the target whole cell is a blood cell and the mixture of whole cells is a blood sample. Claim 18 is fully supported by the specification such as at, for example, page 3, line 28 through page 4, line 6 and Examples 1-13.

No new matter is introduced by these amendments.

§ 112 Rejections

Claim 13 stands rejected under 35 USC § 112, first paragraph, as failing to comply with the written description requirement because claim the subject matter of claim 13 is not a species of the subject matter of claim 12, from which claim 13 depends. The amendment to claim 13 that deletes the phrase, "the azlactone-functional support is a support having a surface comprising azlactone moieties," obviates the rejection.

Furthermore, claim 13 was rejected because, in line 4, "solid plastic particle" was not supported by the specification. Claim 13 has been amended to recite "solid plastic article", which is supported by the specification.

Claims 12-17 stands rejected under 35 USC § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention.

In line 1 of claim 12, the term "interacted support" was objected to as being indefinite as to how "interacted" defines the support. Claim 12 has been amended to define the support as "containing bound target whole cells from a mixture of whole cells."

In line 2 of claim 12, the term "azlactone-functional support" was objected to as being indefinite as to whether the support reacts with an azlactone moiety or contains an azlactone moiety. Claim 12 has been amended to define the support as "comprising one or more base polymer supports containing an azlactone moiety."

In line 4 of claim 12, the term "interacting with" was objected to as being relative and subjective as to phenomena that constitutes interacting. Claim 12 has been amended to recite that target whole cells are "bound to" the biologically active substance.

In line 2 of claim 13, the term "comprising" was objected to as being unclear as to the relationship of the materials recited in the support. Claim 13 has been amended to recite that the support "is in the form of" the recited materials.

In line 1 of claim 16, there was no antecedent basis for "the solid plastic article". The amendment to claim 13 that corrects a typographical error provides antecedent basis for "the solid plastic article."

Applicants submit that the rejections of claims 12-17 under 35 USC § 112, first paragraph, and 35 USC § 112, second paragraph, have been overcome, and that the rejections should be withdrawn.

§ 103 Rejections

Claims 12-17, of which claim 12 is the only independent claim, stand rejected under 35 USC § 103(a) as being unpatentable over U.S. Patent No. 5,993,315 ("Rasmussen") in view of U.S. Pat. No. 6,057,096 ("Rothschild") and U.S. Pat. No. 5,215,927 ("Berenson").

Rasmussen discloses azlactone-functional supports containing a covalently bound ligand for use as an adsorbent to carry out affinity-based separations of compounds from a mixture of compounds. Rothschild and Berenson disclose methods of isolating target cells from a cell mixture.

The Office Action states that it would have been obvious to use as the ligand of Rasmussen a ligand that binds cells and use the bound ligand to separate target cells as suggested by Rothschild and Berenson by using an immobilized ligand that binds the target cells or that binds a complex of the target cells containing a component that binds to the ligand.

While this may or may be true, it is irrelevant to the patentability of Applicants' invention. Assuming, for the sake of discussion, that the recited combination is proper, it fails to teach or suggest all of the limitations of claim 12. Claim 12, as amended herein, recites:

> A support containing bound target whole cells from a mixture of whole cells, comprising:
> (a) a support comprising one or more base polymer supports containing an azlactone moiety,
> (b) a biologically active substance covalently coupled to the support, and
> (c) target whole cells bound to said substance,
> wherein the support comprises one or more base polymer supports that have been identified as exhibiting minimal nonspecific binding of non-target whole cells of the mixture of whole cells.

Applicants' invention is not directed to merely *any* support (e.g., those described in Rasmussen) for whole cell selection. Rather, Applicants' invention involves the

identification of *particular* supports *particularly suited* for whole cell selection because the supports exhibit minimal nonspecific binding of non-target cells in a relevant mixture of whole cells. The suggested combination fails to teach or suggest supports identified as exhibiting minimal nonspecific binding of non-target whole cells of a relevant mixture of whole cells.

The Office Action further states that Applicants' argument that the claims require a species of polymer identified as having minimal nonspecific cell binding is unpersuasive since the polymer of Rasmussen inherently has minimal nonspecific binding for certain types of cells, and that the "nonspecific binding of the claims can be for any cells."

Claim 12 has been amended to recite that the base polymer support is "identified as exhibiting minimal nonspecific binding of *non-target* whole cells of the *mixture of whole cells*." Thus, while the polymers of Rasmussen may, theoretically, exhibit minimal nonspecific binding of *some* cell type, claim 12 as amended herein more particularly defines the cells for which the polymer exhibits minimal nonspecific binding as those cells *relevant* to a particular cell selection – cells of the whole cell mixture that contains the target cells. Moreover, Applicants have demonstrated that polymeric supports can exhibit widely divergent levels of nonspecific binding of non-target cells in, for example, a blood sample (see Table 1). Thus, minimal nonspecific binding of non-target cells in a mixture of cells of whole cells that contains the target cells is not an inherent characteristic of the Rasmussen polymer supports.

The Office Action also states that the "... the prescreening of the claims can result in the same polymer as used by Rasmussen." The fact that some of the supports of the invention may "result in the same polymer as used by Rasmussen" does not render the present claims unpatentable. As Applicants stated in the Preliminary Amendment filed February 28, 2002, a claim to a species within a genus is not rendered obvious and unpatentable by an earlier broad generic disclosure. *In re Baird*, 29 U.S.P.Q.2d 1550 (CAFC 1994). The present invention is properly considered a species of supports - those possessing minimal nonspecific binding for non-target whole cells in a mixture of cells that contain target whole cells - from among the genus of supports

described in Rasmussen. Thus, the present case falls squarely within the precedent established by the CAFC in *In re Baird*.

Finally, the Office Action states, "...there is clear motivation [to identify one or more base polymer supports as exhibiting minimal nonspecific binding of non-target whole cells of the mixture of whole cells] since nonspecific binding of cells is obviously going to result in cells bound being impure." While it may be accurate to state that nonspecific binding of cells results in the bound cells being impure, Applicants respectfully submit that such knowledge would not have provided one of skill in the art motivation to identify base polymer supports with minimal nonspecific binding for non-target cells in the mixture of cells. Prior to Applicants' disclosure, the base polymer supports were not recognized as a source of significantly *controllable* nonspecific binding of non-target cells. Rasmussen does not teach or suggest use of the polymers for whole cell separations. Rothschild teaches recovery of and/or labeling of targets using photocleavable conjugates (see Abstract). Berenson teaches an indirect sandwich technique for immunoselection systems that employs a biotin-conjugated antispecies immunoglobulin that is directed to one or more nonbiotinylated specific antibodies in conjunction with insolubilized avidin (see Abstract). None of the references teaches or suggests that selection of base polymers for the support can significantly control nonspecific binding of non-target cells. Consequently, the references would have failed to motivate on of ordinary skill in the art to identify and select polymers for the support having minimal nonspecific binding for non-target cells in a mixture of cells containing the target cells.

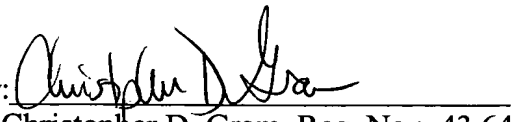
Thus, Applicants assert that claim 12 is patentable under 35 USC § 103(a) over U.S. Patent No. 5,993,315 ("Rasmussen") in view of U.S. Patent No. 6,057,096 ("Rothschild") and U.S. Patent No. 5,215,927 ("Berenson"). Each of claims 13-18 depends, directly or indirectly, from claim 12 and is therefore patentable for at least all of the reasons set forth above regarding the patentability of claim 12. Reconsideration and withdrawal of the rejection is respectfully requested.

Conclusion

In view of the above, Applicants submit that the application is in condition for allowance. Reconsideration of the application and allowance of claims 12-18 is requested.

Respectfully submitted,

March 16, 2004
Date

By: 
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